REMARKS

Further to the Reply filed April 24, 2003, Applicants now amend the claims as indicated above. Support for these claim amendments is found throughout the specification. For example, support for the amendment of claims 1, 2, 10-15, and 23, which now recite 85% sequence identity to particular sequence identifiers (i.e., SEQ ID NOs: 378 and 379), is found in the specification at page 29, lines 1-3, and page 46, line 22 - page 47, line 4.

Applicants have also added new claims 29-49. Support for these claims is found, for example, in claims 1-5, 10-15, 23, 25, and 26, as originally filed, and in the specification at page 29, lines 1-3 (which defines substantial identity as 95% identity to a particular amino acid); page 46, line 22 - page 47, line 4 (which provides SEQ ID NOs: 378 and 379), page 108, line 24 - page 109, line 5 (where Applicants state that the DAF-18 homolog, PTEN, has lipid phosphatase activity); and at page 109, lines 13-15 (where Applicants describe the Cys-$(X)_5$-Arg lipid phosphatase active site).

As presently amended, claims 1-5, 10-15, 23, 25, 26, and 29-35 are free of the written description and enablement rejections asserted by the Office in this case. Claims 1-5, 10-15, 26, and 29-34 provide screening methods to identify compounds that modulate DAF-18 or PTEN expression or activity, and claim 23 and its dependent claims 25 and 35 feature a transgenic *C. elegans* containing a transgene encoding a PTEN polypeptide. These claims now require that the DAF-18 or PTEN polypeptide have at

least 95% amino acid sequence identity to particular sequence identifiers (i.e., SEQ ID NOs: 378 or 379). Given that these claims are now limited to sequences having this very high degree of structural homology to either a *C. elegans* DAF-18 (SEQ ID NO: 379) or PTEN (SEQ ID NO: 378) amino acid sequence, the written description and enablement rejections may be withdrawn.

Similarly, new claims 36-47 provide screening methods to identify compounds that modulate DAF-18 or PTEN expression or activity, and claims 48-49 provide transgenic *C. elegans* containing a transgene encoding a PTEN polypeptide. These methods and compositions require the use of DAF-18 or PTEN polypeptides that have at least 85% amino acid sequence identity to SEQ ID NOs: 378 or 379, possess lipid phosphatase activity, and contain the Cys-$(X)_5$-Arg lipid phosphatase active site. Again, these new claims require a very high degree of structural homology (i.e., 85% sequence identity to SEQ ID NOs: 378 or 379), and, in addition, specify a correlation between structure and function of the polypeptides (i.e., require lipid phosphatase activity and a Cys-$(X)_5$-Arg lipid phosphatase active site). Given the structural and functional requirements of claims 36-49, these claims also satisfy 35 U.S.C. § 112, first paragraph, and should be found to be allowable.

Applicants request reconsideration of the present rejections and allowance of claims 1-5, 10-15, 23, 25, 26, and 29-49.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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